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From

Department of Chemistry

Duke University

Durham, North Carolina

Final Report

Certain Reactions of Organometallic
Compounds and Some Cyclizations

Contract No. DA-36-034-ORD-2040

for the period 1 September 1955 - 31 December 1962

Submitted by Charles R. Hauser
Chief Investigator

1963

NO OTS

The first section of this report lists the titles the reports issued during the period 1 July 1955 - 31 August 1959. The second section lists additional reports issued during the latter part of contract along with a discussion of work still in progress.

Reports:

1. Acylations of Nitriles with Esters by Sodium Amide in Liquid Ammonia to Form β -Ketonitriles. Consideration of Amide Formation, by Charles J. Eby and C.R. Hauser, in J Am Chem Soc, 79 (1957), p 723-725. AD-137 004
2. Cyclization of β -Ketonitriles or β -Ketoamides with Ketones by Polyphosphoric Acid to Form Substituted 2-Pyridones, by C.R. Hauser and Charles J. Eby, in J Am Chem Soc, 79 (1957), p 728-731. AD-137 005
3. The Conversion of β -Ketonitriles to β -Ketoamides by Boron Fluoride in Aqueous Acetic Acid by Polyphosphoric Acid, by C.R. Hauser and Charles J. Eby, in J Am Chem Soc, 79 (1957), p 726-727. AD-137 006
4. Aminomethylation of Ferrocene to Form N,N-Dimethylaminomethylferrocene and Its Conversion to the Corresponding Alcohol and Aldehyde, by Jacques K. Lindsay and C.R. Hauser, in J Org Chem, 22 (1957), 355-358. AD-137 002
5. Certain Acylations of Ferrocene and Some Condensations Involving the α -Hydrogen of Acetylferrocene, by C.R. Hauser and Jacques K. Lindsay, in J Org Chem, 22 (1957), p 482-485. AD-137 007
6. Some Typical Aldehyde Addition and Condensation Reactions of Formylferrocene, by C.R. Hauser and Jacques K. Lindsay, in J Org Chem, 22 (1957), p 906-908. AD-137 008
7. N- and C-Benzoylation of *p*-Aminoacetophenone with Methyl Benzoate by Sodium Amide. Synthesis of β -Diketones Having *p*-Acylamino and *p*-Hydroxy Groups, by C.R. Hauser and Charles J. Eby, in J Org Chem, 22 (1957), p 909-912. AD-137 011
8. A Novel Ring Enlargement Involving the ortho Substitution Rearrangement by Means of Sodium Amide in Liquid Ammonia, by Daniel Lednicer and C.R. Hauser, in J Am Chem Soc, 79 (1957), p 4449-4451. AD-137 012
9. Some Reactions of the Methiodide of N,N-Dimethylaminomethylferrocene, by C.R. Hauser and others. (Ms sub to J Org Chem).

10. Certain Alkylations with the Methiodide of N,N-Dimethylaminomethylferrocene. Synthesis of an α -Amino Acid Having the Ferrocene Group, by C.R. Hauser and Jacques K. Lindsay, in J Org Chem, 22 (1957), p 1246-1247. AD-137 013
11. Rearrangement of 2,4,6-Trisopropylbenzyltrimethylammonium Ion by Sodium Amide to Form an exo-Methylenecyclohexadieneamine and Its Reactions, by Donald N. Van Eenam and C.R. Hauser, in J Am Chem Soc, 79 (1957), p 5520-5524. AD-137 014
12. Reaction of 9-Bromomethylenefluorene with Potassium Amide in Liquid Ammonia Dimerization, by C.R. Hauser and Daniel Lednicer, in J Org Chem, 22 (1957), p 1248-1250. AD-137 015
13. Conjugate Addition Condensations of Diphenylmethane Involving Methylene Hydrogen by Potassium Amide. Cyclizations of Products by Polyphosphoric Acid, by Marvin T. Tetenbaum and C.R. Hauser, in J Org Chem, 23 (1958), p 229-233. AD-137 067
14. Condensations of Benzhydrylmethyl Ether Involving α -Hydrogen by Potassium Amide. Cyclization of Conjugate Addition Product by Polyphosphoric Acid, by C.R. Hauser and Marvin T. Tetenbaum, in J Org Chem, 23 (1958), p 233-235. AD-137 069
15. The ortho Substitution Rearrangement and Certain Related Reactions in the Naphthylene Series by Sodium Amide, by C.R. Hauser, Donald N. Van Eenam and Phillip L. Bayless, in J Org Chem, 23 (1958), p 354-358. AD-137 070
16. Reaction of the Methiodide of N,N-Dimethylaminomethylferrocene with Potassium Cyanide to Form Ferrocylacetonitrile, by Daniel Lednicer, Jacques K. Lindsay and C.R. Hauser, in J Org Chem, 23 (1958), p 653-655.
17. Rearrangement of the Methiodide of N,N-Dimethylaminomethylferrocene by Potassium Amide in Liquid Ammonia, by C.R. Hauser, Jacques K. Lindsay and Daniel Lednicer, in J Org Chem, 23 (1958), p 358-360. AD-137 068
18. Five- vs. Six-Membered Ring Formation in the Cyclization of 2,3,4-Triphenylbutyric Acid; the Relative Importance of Stereochemistry, by Daniel Lednicer and C.R. Hauser, in J Am Chem Soc, 80 (1958), p 3409-3412. AD 201 869

19. α,β -Diphenylbutyronitrile (Erythro Isomer), by C.R. Hauser and W.R. Dunnivant. (Ms sub to Org Synthesis).
20. α,α,β -Triphenyl Propionitrile, by C.R. Hauser and W.R. Dunnivant. (Ms sub to Org Synthesis).
21. α,β -Diphenylpropionic Acid, by C.R. Hauser and W.R. Dunnivant. (Ms sub to Org Synthesis).
22. α,α,β -Triphenylpropionic Acid, by C.R. Hauser and W.R. Dunnivant. (Ms sub to J Org Chem).
23. Reductive Metalation of Benzophenone and Benzalacetophenone by Alkali Metals in Liquid Ammonia and Some Condensations of the Resulting Dialkali Salts, by Phillip J. Hamrick, Jr. and C.R. Hauser, in J Am Chem Soc, 81 (1959), p 493-496.
24. Alkylations of Certain Carbanions with 1-Chloro-1,2-Diphenylethane. β -Eliminations with Other Bases, by C.R. Hauser, Charles F. Hauser and Phillip J. Hamrick, Jr., in J Org Chem, 23 (1958), p 1713-1714. AD 210 148
25. The Benzal Derivative of Ferrocenylacetonitrile, by C.R. Hauser and Charles E. Cain, in J Org Chem, 23 (1958), p 2006-2007.
26. The Methiodide of N-(4-benzyloxy-2,6-dimethylbenzyl)-N,N-Dimethylamine. Attempted Rearrangement, by Daniel Lednicer and C.R. Hauser, in J Org Chem, 23 (1958), p 2008-2009.
27. Hydroxymethyl- and Formylferrocene with Oxidizing Agents. Bisferrocenylmethyl Ether, by C.R. Hauser and Charles E. Cain, in J Org Chem, 23 (1958), p 2007-2008.
28. Five- vs. Six-Membered Ring Formation in Acid Catalyzed Cyclizations. II. 3,4-Diphenylvaleric Acid and 2,3-Diphenylglutaric Acid, by Daniel Lednicer and C.R. Hauser, in J Am Chem Soc, 80 (1958), p 6364-6367. AD 210 831
29. The Structure of the Product of the Anomalous Leuckart Reaction of 2-Ferrocylethylamine. A Route to 1,2-Disubstituted Ferrocenes, by Daniel Lednicer and C.R. Hauser, in J Org Chem, 24 (1959), p 43-46. AD 137 099

30. Addition Reactions of the Methiodide of Benzophenomethylimine and Its 4-Methyl Analogue with Nucleophilic Reagents, by C.R. Hauser and Daniel Lednicer, in J Org Chem, 24 (1959), p 46-49.
31. N-Ferrocylmethyl-N,N,N-Trimethylammonium Iodide (Methiodide of N,N-Dimethylaminomethylferrocene), by C.R. Hauser. (Ms sub to Org Synthesis).
32. Two-Fold Alkylations of Sodium Diphenylmethide with Methylene Halides to Form bis-Benzhydrylmethylene Hydrocarbons. Alkylations of Sodium Triphenylmethide, by C.R. Hauser, Charles F. Hauser and Phillip J. Hamrick, Jr, in J Org Chem, 24 (1959), p 397-400.

Final Report for Contract with Army Research Office (Durham) for
period September 1, 1959 to December 31, 1962

By Charles R. Hauser
Duke University, Durham, N. C.

"Certain Reactions of Organometallic Compounds and Some Cyclizations"

(A) Publications.-- The eighteen original articles listed below were published or were accepted for publication during the three year and four month period, September 1, 1959 to December 31, 1962. Fifteen of the eighteen articles are papers, one is a communication and two are notes, the communication and notes being indicated. Ten of the articles were supported wholly by the Army Research Office (Durham)), and five in part by this Office. Also, five Preparations were published in Organic Syntheses; these are listed under titles 19-23.

1. "Condensation of Phenylacetic Acid with Certain Ketones to Form alpha-Phenyl-beta-hydroxy Acids by Alkali imides. Equilibrium Factors," P. J. Hamrick, Jr. and C. R. Hauser, J. Am. Chem. Soc., 82, 1957-1959 (April, 1960).

2. "Synthesis of beta-Hydroxy Esters from Ethyl Acetate and Ketones or Aldehydes by Means of Lithium Amide. Some Results with other Esters," W. R. Dunnivant and C. R. Hauser, J. Org. Chem., 25, 503-507 (April, 1960).

3. "2-Acetyl-6-methoxycoumaran-3-one. Benzylolation at the Terminal Methyl Groups," W. I. O'Sullivan and C. R. Hauser, J. Org. Chem., 25, 839-840 (1960)(A Note).

4. "Certain Condensations at the Terminal Methyl Group of 3-Phenylpentane-2,4-dione through Its Dipotassio Derivative Cyclizations," W. I. O'Sullivan and C. R. Hauser, J. Org. Chem., 25, 1110-1114, (July, 1960).
5. "Factors in Aldol Condensations of Alkyl Acetates with Benzophenone and Reversals by Sodium Amide Versus Lithium Amide. C. R. Hauser and W. R. Dunnivant, Metallic Cation Effects," J. Org. Chem., 25, 1296-1302 (August, 1960)
6. "Condensation of Alkyl Acetates with Benzophenone by Lithium Amide to Form beta-Hydroxy Esters. Relative Ease of Self-condensation of Esters," W. R. Dunnivant and C. R. Hauser, J. Org. Chem., 25, 1693-1699 (October, 1960).
7. "Alkali Catalyzed Aldol Condensation of Bisacetylferrocene with Benzaldehyde to Form Mono- and Dibenzaldehyde Derivatives," T. A. Mashburn, Jr., C. E. Cain, and C. R. Hauser, J. Org. Chem., 25, 1982-1986 (November, 1960).
8. "Acylation of Bisacetylferrocene with Esters by Potassium Amide to Form Bis-beta-diketones. Consideration of Mechanism," C. E. Cain, T. A. Mashburn, Jr., and C. R. Hauser, J. Org. Chem., 26, 1030-1034 (April, 1961).
9. "Influence of the Metallic Cation of Certain Organometallic Compounds on the Courses of Some Organic Reactions," W. I. O'Sullivan, F. W. Swamer, W. J. Humphlett, and C. R. Hauser, J. Org. Chem., 26, 2306-2310 (July, 1961).
10. "Some Condensations at the Methylene and Terminal Methyl Groups of Benzenesulfonylacetone Through its Mono- and Dipotassio Salts," W. I. O'Sullivan, D. F. Tavares and C. R. Hauser, J. Am. Chem. Soc., 83, 3453-3457 (August, 1961).

11. "Reactions of Alkali Diphenylmethides with Certain Polyhalides. Displacement on Halogen or Hydrogen," C. R. Hauser, W. G. Kofron, W. R. Dunnivant, and W. F. Owens, J. Org. Chem., 26, 2627-2629 (August, 1961).
12. "2-, 3-, and 4-Lithiobenzyltrimethylamines. Grignard Reagent of 2-Bromobenzyltrimethylamine," F. N. Jones and C. R. Hauser J. Org. Chem., 27, 701 (October, 1961) (A Communication).
13. "Acetylation of Benzenesulfonylacetone with Acetic Anhydride by Means of Boron Fluoride to Form the Terminal Methyl Derivative," D. F. Tavares, W. I. O'Sullivan, and C. R. Hauser, J. Org. Chem., 27, 1251-1254 (April, 1962).
14. "Ortho-Substitution Rearrangement vs. Elimination Reaction of Certain Benzyl-Type Quaternary Ammonium Ions with Sodium Amide," F. N. Jones and C. R. Hauser, J. Org. Chem., 27, 1542-1547 (May, 1962).
15. "Synthesis of 3-Substituted 3-Phenylphthalides," F. N. Jones and C. R. Hauser, J. Org. Chem., 27, 3364 (April, 1962) (A Note).
16. "Ortho Substitution Rearrangement vs. Elimination Reaction of Ring-substituted Benzyltrimethylethylammonium Ions," F. N. Jones, and C. R. Hauser, J. Org. Chem., 27, 4020-4024 (November, 1962).
17. "Halogen-metal Interchange of 2-, 3-, and 4-Bromobenzyltrimethylamines with *n*-Butyllithium. Grignard Reagent of 2-Bromobenzyltrimethylamine," F. N. Jones and C. R. Hauser, J. Org. Chem., (In Press).

18. "Metalations of Benzyldimethylamine and Related Amines with n-Butyllithium in Ether. Deuteration to Form Ring and Side-chain Derivatives," F. N. Jones, M. F. Zinn, and C. R. Hauser, J. Org. Chem., (In Press).

19. α,α,β -TRIPHENYLPROPIONITRILE, C. R. Hauser and W. R. Dunnivant, Organic Syntheses, 39, 73-74 (1959).

20. N,N-DIMETHYLAMINOMETHYLFERROCENE METHIODIDE, D. Lednicer and C. R. Hauser, Organic Syntheses, 40, 31-33 (1960).

21. α,β -DIPHENYLPROPIONIC ACID, C. R. Hauser and W. R. Dunnivant, Organic Syntheses, 40, 38-40 (1960).

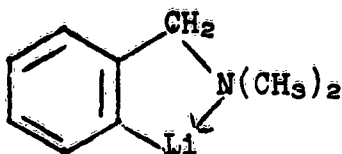
22. FERROCENYLACETONITRILE, D. Lednicer and C. R. Hauser, Organic Syntheses, 40, 45-46 (1960).

23. HYDROXYMETHYLFERROCENE, L. Lednicer, T. A. Mashburn, Jr., and C. R. Hauser, Organic Syntheses, 40, 52-53 (1960).

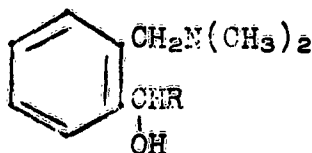
(B) Work in Progress. - This work is considered below under appropriate titles (1-4). The completeness of each of the problems is indicated in the outline. We anticipate that these problems will be completed under the new grant.

1. "Condensation of Aldehydes, Ketones and Other Compounds at the Ortho Position of Benzyldimethylamine and Related Amines by Means of n-Butyllithium."

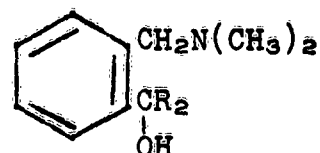
Benzyldimethylamine was converted by n-butyllithium in ether to the ortho lithio intermediate I, which was condensed with benzaldehyde and certain substituted benzaldehydes to form II and with benzophenone and acetone to give III. The yields were good.



I

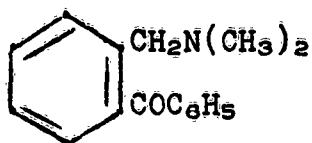


II

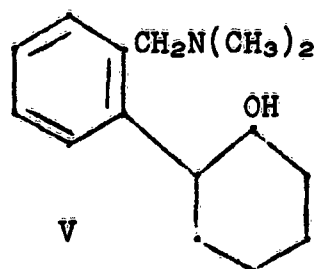


III

Also I was condensed with benzonitrile to afford IV (77%) and with cyclohexene oxide to give the ortho derivative V (36%).

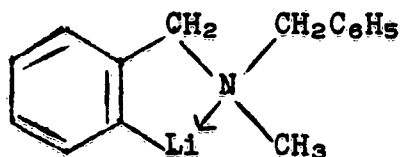


IV

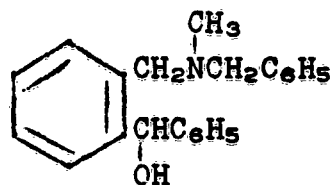


V

Similarly dibenzylmethylamine was metalated with *n*-butyllithium to form the ortho lithio intermediate VI, which was condensed with benzaldehyde to give the ortho derivative VII (56%).

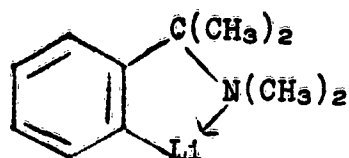


VI

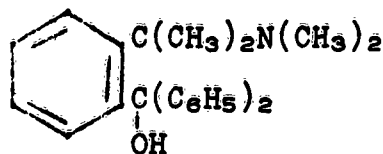


VII

Likewise α,α -dimethylbenzylidimethylamine was metalated with *n*-butyllithium to form the ortho lithio intermediate VIII, which was condensed with benzophenone to give IX (57%).



VIII

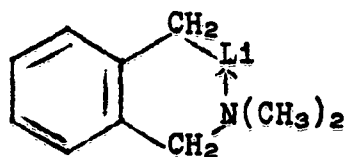


IX

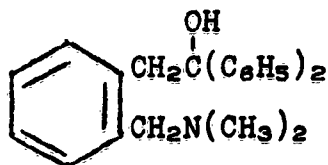
Certain other metalations and condensations have been effected but the structures of the products have not yet been established. Some related reactions are contemplated.

2. "Condensations of Aldehydes and Ketones at the Side-chain of 2-Methylbenzylidimethylamine and Related Amines by Means of n-Butyllithium."

2-Methylbenzylidimethylamine was metalated at the methyl side-chain with n-butyllithium in ether to form the lithio intermediate I, which was condensed with benzaldehyde, acetone and benzophenone to give, for example, II. Mixtures of products were obtained with the first two compounds but benzophenone afforded II in 82% yield, though the structure of this product has not yet been definitely established.

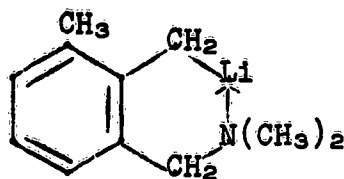


I

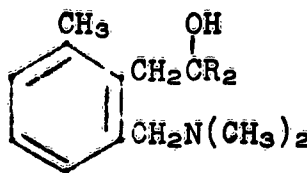


II

Similarly 2,3-dimethylbenzylidimethylamine was metalated with n-butyllithium to form III, which was condensed with benzophenone and acetone to give IV where R is phenyl and methyl, respectively. The yields were good.



III



IV

Also tertiary amine V was metalated with n-butyllithium to form apparently VI which reacted with benzophenone to give VII (35%) though the structure of this product has not yet been established.

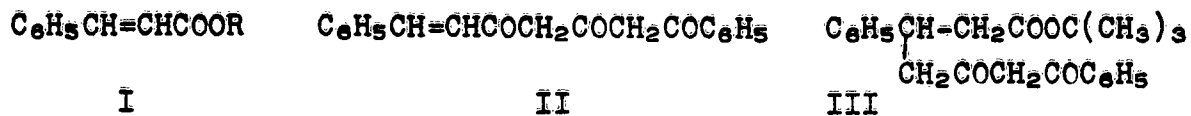


Further studies are being made on such side-chain metalations and condensations.

3. "Carbonyl Versus Conjugate Addition of Dipotassio-β-Di-ketones with Cinnamic Esters."

It has recently been shown that dipotassiobenzoylacetone undergoes carbonyl addition with chalcone but conjugate addition with 2,4,6-trimethylchalcone (R. J. Light, T. M. Harris and C. R. Hauser, J. Org. Chem., 26, 1344 (1961)).

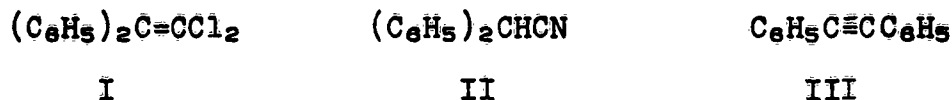
It has now been found that dipotassiobenzoylacetone can be made to undergo either carbonyl or conjugate addition with cinnamic esters, the course of reaction depending on the R group in the alkoxy or aryloxy portion of the ester I. Thus carbonyl addition occurs with phenyl cinnamate to form II (55%), whereas conjugate addition takes place with t-butyl cinnamate to give III (70%). Both courses of reaction occur with methyl cinnamate.



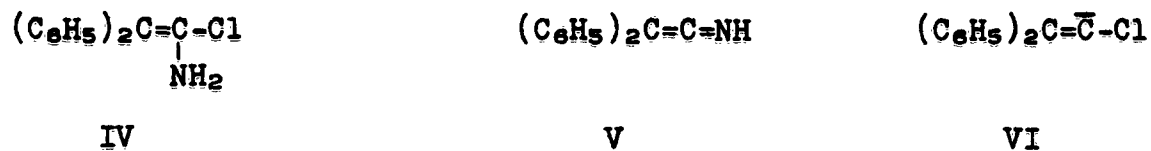
The structures of the products are being established, and certain related reactions are being studied.

4. "Reactions of 1,1-Dichloro-2,2-diphenylethylene with Nucleophilic Reagents."

1,1-Dichloro-2,2-diphenylethylene (I) has been found to react with potassium amide in liquid ammonia to form diphenylacetonitrile (II, 90%) but with phenyllithium in ether to give tolane (III, 67%) and chlorobenzene (71%).



The former reaction appears to involve substitution at the vinylic carbon to form IV, which undergoes β -elimination to give V and subsequently the anion of II. The reaction with phenyllithium evidently involves displacement on halogen to form chlorobenzene and carbanion VI, which undergoes rearrangement to afford tolane.



The reactions of I with certain other nucleophilic reagents are being studied. Also certain related reactions are contemplated.

(C.) Research Personnel and Degrees Awarded.- The following graduate students were supported on the contract for a few months to a year: W. R. Dunnavant, F. N. Jones, T. A. Mashburn, and R. L. Vaulx. The first three of these men completed the research for the Ph.D. thesis while on the contract. The last man is presently a third year graduate student who has been on the contract since last September.

The following post-doctoral fellows were supported on the contract for a year each: W. I. O'Sullivan, D. F. Tavares, F. N. Jones and F. B. Kirby. During the academic year, Drs. O'Sullivan and Jones were supported partly by Duke University, since they were part-time instructors of chemistry. This made contract funds available for securing Dr. Kirby, who started work last January (1962).